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EXAMINER

IBRAHIM, MEDINA AHMED

ART UNIT PAPER NUMBER

1638

DATE MAILED: 07/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n N .

10/047,825

Applicant(s)

DUVICK ET AL.

Examiner

Medina A Ibrahim

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-- The MAILING DATE of this c mmunication appears n the cover sheet with th c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 6-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 January 2002 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 2-5, and invention (B) in Paper No. 8 filed on 4/11/03 is acknowledged. The restriction requirement is made FINAL.

Claims 1-43 are pending.

Claims 1 and 6-43 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 2-5 are under examination.

Information Disclosure Statement

2. Initialed and dated copy of the IDS form 1449 of Paper no. 6 is attached to the instant Office action.

Drawings

3. The drawings filed on 1/16/2002 are approved by the Examiner.

Specification

4. The disclosure is objected to because of the following informalities: for example, page 16, line 23, contains an embedded hyperlink directed to an Internet address. The use of hyperlinks and/or other form of browser- executable code are not permitted under USPTO current policy because the content of such links are subject to a change, resulting in the introduction of New Matter into the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser- executable code. See MPEP 608.01.

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Claim Objections

2. Claims 2-5 are objected to because of the following informalities. The claims recite SEQ ID NO: 1-2 and 5-37, drawn to non-elected inventions. The claims should be amended accordingly.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 2-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 5, in part (e), recite "stringent conditions" without specific hybridization and wash conditions. There are many different meanings of the phrase. Applicant has not clearly defined the appropriate was/hybridization conditions, and hence it is not known what is encompassed by the claim. Appropriate correction is required to more clearly define the metes and bounds of the claimed invention.

Claims 2 and 5 are indefinite in the recitation of "peroxidase-like" activity in parts (c, d, and e). The term is not clearly defined in the specification, and hence what is encompassed by the claim is unclear. It is unclear how the "peroxidase-like" activity differs from "peroxidase" activity, or how it is "like" a peroxidase. If Applicant intends the peroxidase activity of SEQ ID NO: 4, then "peroxidase-like" should be replaced with ---peroxidase---. Dependent claims 3-4 are included in the rejection.

Claim Rejections - 35 USC § 112, Scope of enablement

5. The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 3 or a nucleotide sequence encoding the polypeptide having the amino acid sequence of SEQ ID NO: 4, an expression vector comprising said nucleic acid molecule, and a host cell stably transformed with said vector, does not reasonably provide enablement for any nucleotide sequence comprising at least 16 contiguous bases of a nucleotide sequence encoding SEQ ID NO:4, any nucleotide sequence having at least 60% sequence identity to SEQ ID NO:3, any nucleotide sequence that hybridizes to SEQ ID NO:3 under any stringent conditions, and encoding a polypeptide having peroxidase-like activity, and a host cell stably transformed with said nucleotide sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a nucleic acid molecule comprising any nucleotide sequence from any source comprising at least 16 contiguous bases of SEQ ID NO: 3, having at least 60% sequence identity to SEQ ID NO: 3, or that hybridizes to SEQ ID NO: 3 under unspecified stringent conditions, and encoding a polypeptide having peroxidase-like activity, a promoter operably linked to said nucleotide sequence.

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The claims are also drawn to an expression vector comprising the nucleic acid molecule of the invention and a host cell stably transformed with said vector.

Applicant teaches isolation of cDNAs from maize and the isolated nucleotide sequence of SEQ ID NO: 3 encoding the polypeptide sequence of SEQ ID NO: 4. Applicant teaches that SEQ ID NO: 3 encoding SEQ ID NO: 4 has peroxidase activity and shares approximately 82.7% sequence identity with a peroxidase from *Cenchrus ciliaris* (NCBI Accession No. AAA20472). Applicant further teaches that this peroxidase sequence from maize also shares sequence identity with peroxidases from *Gossipyum hirsutum*, flax, tobacco, and *scutellaria baicalensis*, known in the art (page 51, Example 5). Applicant teaches that the expression of SEQ ID NO: 3 is induced during defense response (Example 8). Applicant shows that the expression levels of the maize peroxidases in maize are increased following infections by *Fusarium* species, *C. carbonum*, *Cochlibolus heterostrophus*, and by the avirulence gene AvRxv (Examples 6-7 and 9-10). Therefore, SEQ ID NO: 3 encoding SEQ ID NO: 4 has antipathogenic activity in plant cells.

Applicant has not provided guidance for how to identify or obtain all nucleotide sequences having both the structural and functional limitations as recited in the claims. The breadth of the claims encompasses nucleotide sequences obtainable by modifications including multiple deletions and/or substitutions of nucleotides in SEQ ID NO: 3. However, Applicant has not taught which regions in SEQ ID NO: 3 would tolerate such modifications. Applicant has not taught which 16 contiguous bases has the ability to encode a functional polypeptide having the desired activity. Therefore, Applicant has

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not provided guidance for modifications to SEQ ID NO: 3 that resulted nucleotide sequences having both the structural and functional limitations as recited in claims 2 and 5, (parts c-d).

While mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims. One skilled in the art would expect any tolerance to modification for a given DNA/protein to diminish with each further and additional modification or multiple substitutions/deletions. One skilled in the art would have to make all possible nucleotide substitutions and deletions in the 1354 nucleotide long sequence of SEQ ID NO: 3 and test all nucleotide sequences that meets the structural limitations to determine which also meet the functional limitation.

The state of the prior art teaches unpredictability inherent in DNA/protein function if one or more amino acids/bases in that DNA/protein are modified. For example, Lazar et al (Molecular and Cellular Biology, March 1988, Vol. 8, No. 3, pp. 1247-1257 (U)) teach that a mutation of aspartic acid 47 and leucine 48 of a transforming growth factor alpha results in different biological activities (see at least the Title). Broun et al (Science, 13 November 1998, vol. 282, pp. 131-133 (U)) teach that as few as four amino acid substitutions in a protein can change the protein activity (Abstract). Note, the nucleotide sequences encoding the proteins (mutated and original) disclosed by either Lazar or Broun would share more than 60% sequence identity and would hybridize to each other under any stringent conditions. Therefore, it is unpredictable if any nucleotide sequence having at least 60% to SEQ ID NO: 3 and any nucleotide sequence that hybridizes

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thereto under unspecified stringent conditions would encode a polypeptide having the desired peroxidase activity.

Further, the state of the prior art further teaches complexity of the peroxidase gene family with respect to their large and variable number of isozymes, and identification of peroxidase genes implicated in plant defense response (see P. Simon, Plant Peroxidase Newsletter, no.1, pp. 1-6, February 1993). The paragraph bridging pages 2 and 6 discusses the plant peroxidases as follows: "Plant peroxidases are reputed for their large and variable number of isozymes.... Isozymic profiles are often flexible and can reflect genetic diversity, posttranslational modifications, physiological conditions and extraction artifacts. Furthermore, this apparent intraspecies diversity is complicated by interspecies variations."

In addition, since the working example disclosed in the specification is limited to unmodified SEQ ID NO: 3, the ability of SEQ ID NO: 3 to encode a polypeptide having peroxidase activity cannot be extrapolated to any variant thereof, absent specific guidance.

Therefore, given the breadth of the claims, the nature of the invention, the unpredictability in the art with respect to DNA/protein modifications, the limited guidance and working examples in the specification as discussed supra, and the state of the prior art, the claimed invention is not enabled throughout the broad scope. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

See, also, *Amgen Inc. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1027 (Fed. Cir. 1991) where the court held that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Written Description

7. Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any nucleic acid molecule comprising any and all nucleotide sequences from any source comprising at least 16 contiguous bases of SEQ ID NO: 3, any and all nucleotide sequences having at least 60% sequence identity to SEQ ID NO: 3, any and all nucleotide sequences that hybridize to SEQ ID NO: 3 under unspecified stringent hybridization conditions, and encoding a polypeptide having peroxidase-like activity, and a promoter operably linked to said nucleotide sequence. The claims are also drawn to an expression vector comprising the nucleic acid molecule and a host cell stably transformed with said vector. In contrast, Applicant describes SEQ ID NO:3 and nucleotide sequences encoding SEQ ID NO:4, and other maize peroxidases having pathogen inducible activity. These are genus claims.

See, *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997) where it states "A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to

members of the genus, which features constitute a substantial portion of the genus. See also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. See, also Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

Applicant has not described all nucleotide sequences from any source having at least 60% sequence identity to SEQ ID NO: 3, or that hybridize to SEQ ID NO: 3 under stringent conditions and nucleotide sequences comprising any 16 contiguous bases of SEQ ID NO: 3, and still encoding a polypeptide having peroxidase-like activity. One would not expect that the majority of the nucleotide sequences that share 16 contiguous bases of SEQ ID NO: 3 or those that share 60% sequence identity therewith to encode a polypeptide having the activity of SEQ ID NO: 4. The hybridizing sequences are expected to vary because "stringent conditions" (is open to individual interpretations) will yield unrelated nucleotide sequences. Therefore, a substantial variation in structures and function is expected among the claimed nucleotide sequences. Therefore, the disclosure of SEQ ID NO: 3 and nucleotide sequences encoding SEQ ID NO: 4, and other maize peroxidases isozymes described in the specification are not a representative species of the genus of the claims. Therefore, the specification fails to adequately describe the nucleotide sequences of claims 2 and 5, (parts c, d, and e). Consequently, the specification has not provided an adequate description for

expression vectors comprising said sequences and host cells transformed with said vector. Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that Applicant was in possession of the invention as broadly claimed at the time of filing.

Therefore, weighing all factors above, the claimed invention does not meet the current written description requirements.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Shen et al (Accession no. T18410, Oct. 1996).

The claim is directed to a nucleotide sequence that comprises at least 16 contiguous bases of SEQ ID NO: 3, or hybridizes thereto under stringent conditions, and encoding a polypeptide having peroxidase-like activity. SEQ ID NO: 3 is from maize. The claim does not recite specific hybridization/wash conditions, and the specification does not clearly define "stringent conditions". Note, "peroxidase-like" activity is interpreted here as "peroxidase".

Shen et al teach an isolated cDNA, from maize comprising at least 150 contiguous bases of SEQ ID NO: 3, encoding a polypeptide having peroxidase activity

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(Accession No. T18410, Sequence Search Result, pages 3-4); said cDNA inherently hybridizes to SEQ ID NO: 3 under stringent conditions. Therefore, Shen anticipates claim 2.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 2-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ross, A.H, (Accession No. U12314; Thesis, Botany, University of Queensland).

The claims are drawn to an isolated nucleic acid molecule comprising a nucleotide sequence having at least 16 contiguous bases of SEQ ID NO: 3 encoding a polypeptide having a peroxidase-like activity, and a heterologous promoter that derives

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expression in a plant cell, an expression vector comprising the nucleic acid molecule and a host cell stably transformed with said vector.

Ross teaches an isolated gene that comprises at least 60 contiguous bases of SEQ ID NO: 3 and encoding a polypeptide having peroxidase activity (see Accession No. U12314, Sequence Search Result, pages 1-2). On page 134 of the thesis, last paragraph, Ross suggests cloning the peroxidase gene into a plant expression vector comprising a desired promoter that directs expression in plant tissues, and transforming buffel grass tissues with the vector to produce stably transformed plant/plant tissues.

Ross does not expressly teach a stably transformed plant cell expressing peroxidase.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to transform a plant host cell with a peroxidase gene including the peroxidase gene disclosed by Ross, to produce a stably transformed plant cell as suggested by Ross, with a reasonable expectation of success. One having ordinary skill in the art would have been motivated to do this, given the importance of peroxidases in plant defense system and in modification of lignin for improved nutritional quality as taught by Ross (paragraph bridging pages 131 and 132). Therefore, the claimed invention as whole was clearly a prima facie obvious. Note, "peroxidase-like" activity is interpreted here as "peroxidase" activity.

Remarks

12. The nucleotide sequence of SEQ ID NO: 3 and nucleotide sequences encoding SEQ ID NO: 4 are deemed free of the prior art of record.

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No claim is allowed.

13. Papers related to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmission 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Medina A. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday-Thursday from 8:30AM to 5:30PM and every other Friday from 9:00AM to 5:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

6/26/03

Mai

